Patient Preferences of Health State Utilities Associated with Glycemic Variability in People Living with Type 1 and Type 2 Diabetes

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BACKGROUND AND OBJECTIVE

- Several novel molecules have been designed as once-weekly basal insulins.[1,2]
- Pharmacokinetic profiles suggest that weekly insulin medications currently under investigation may differ in glycemic variability (GV), which refers to oscillations in blood glucose levels within and between days.[3]
- High GV has been associated with poor quality of life in patients with diabetes,[4,5] and reduced GV has been associated with improved health utility among patients with type 2 diabetes (T2D) initiating insulin pump therapy.[6] However, there are no known utility values associated with GV among patients with type 1 diabetes (T1D) or type 2 diabetes receiving treatment with injectable insulin.
- Cost-effectiveness analyses will be needed to examine the value of new weekly insulin treatments to inform healthcare resource allocation decision-making, and these cost-effectiveness analyses will require health state utilities representing differences among these treatments.
- **The purpose of this study was to examine preferences and estimate utility differences associated with glycemic variability (GV) among people with T1D and T2D.**

CONCLUSIONS

- Findings suggest that differences in GV are important to people with T1D and T2D, even when blood glucose remains within the target range.
- The health state utilities estimated in this study may be useful in cost-effectiveness models evaluating weekly insulins that differ in GV.

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METHODS

Study Design
- Health state utilities associated with GV were estimated in a vignette-based time trade-off (TTO) utility elicitation study.
- In-person interviews with respondents with T1D and T2D were conducted in three locations in the United Kingdom (Manchester, London, and Edinburgh) in April 2024.

Participants
- All participants were required to be ≥18 years old; have had a diagnosis of T1D or T2D for at least 6 months; and currently receiving medication for their diabetes and to provide proof of this treatment (e.g., a photo of their medication or a prescription note).

Health State Vignettes
- Health state vignettes were developed for valuation by people with T1D and T2D. All health states included a description of diabetes, blood glucose levels that are generally in control, and weekly basal insulin in combination with mealtime insulin (T1D) or oral medication (T2D).
- The vignettes varied with regard to GV (see sample health states in **Figure 1**).
- The low GV health state described blood glucose levels that are "mostly steady within the target range." The high GV health state described morning blood glucose that "varies from day-to-day" within target range and times when blood glucose levels are "higher or lower" within the target range throughout the day.
- Descriptions of high and low GV were always within the respondent's target blood glucose range so that the resulting utilities would represent preferences associated with variability in blood glucose, rather than hypoglycemia or hyperglycemia.
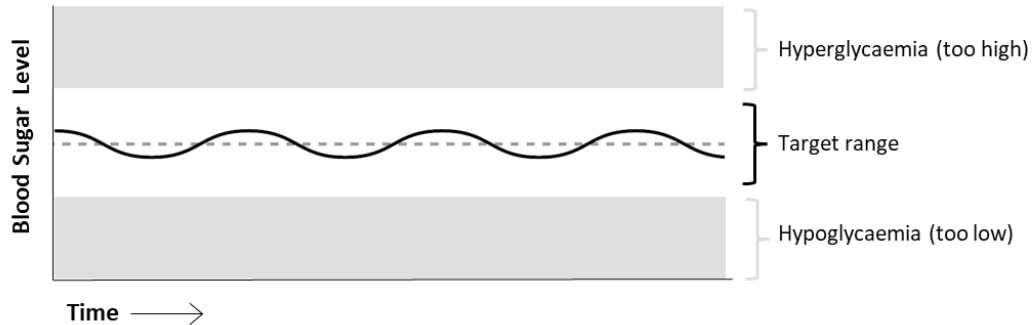
Pilot Study
- A pilot study was conducted to finalize the interview procedures and health state descriptions. The pilot sample included 26 participants with T1D (n=8; mean age = 28.9 years; 50% female) or T2D (n=18; mean age = 49.7 years; 50% female).
- Minor revisions were made to the health states based on participant feedback to improve clarity, particularly around the description of GV to ensure participants understood that blood glucose variability did not refer to hypoglycemia or hyperglycemia.
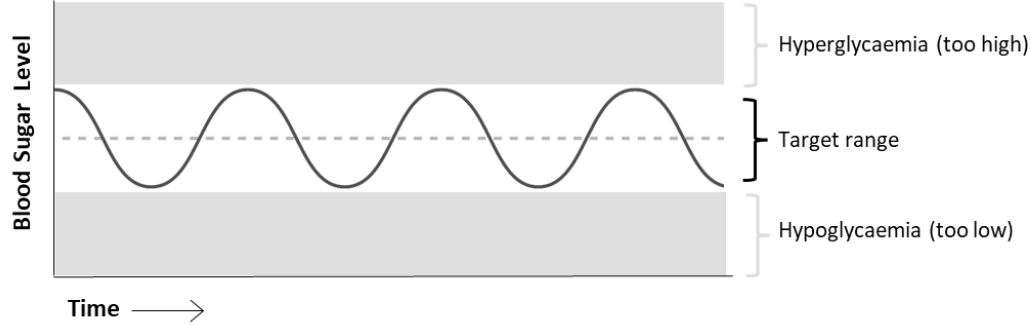
Procedures
- Participants first completed an introductory ranking task and rated their preference for weekly basal insulin with low GV or high GV on a 7-point scale ranging from "strongly prefer mostly steady within target range" to "strongly prefer varies within target range."
- Participants valued the GV health states in a TTO task with a 20-year time horizon and 5% (1 year) trading increments.

HEALTH STATES

Figure 1. Sample GV Health States (T1D)

Diabetes	You have had type 1 diabetes for several years. This means that your body does not produce insulin. / Insulin is a naturally occurring substance that controls the amount of sugar in your body.
Blood Sugar	In order to maintain control of your diabetes, you manage your blood sugar level through medication, diet, and exercise. / Your blood sugar mostly stays within a target range that is not considered hypoglycaemia (too low) or hyperglycaemia (too high). / ○ If your blood sugar level is too low, you may experience dizziness/light-headedness, sweating, or shaking. / ○ If your blood sugar level is too high, you may experience tiredness, blurred vision, thirst, or frequent urination.
Mealtime Insulin	You give yourself insulin injections around mealtimes.
Long-Acting Insulin (once each week)	You give yourself an injection of long-acting insulin once each week.
Blood Sugar Fluctuations (mostly steady within target range)	Your blood sugar levels are generally in control with your insulin. / Your morning blood sugar is generally within your target range and similar from day to day. / Your average blood sugar levels are good, and throughout the day, your blood sugar levels are mostly steady within your target range.

Diabetes	You have had type 1 diabetes for several years. This means that your body does not produce insulin. / Insulin is a naturally occurring substance that controls the amount of sugar in your body.
Blood Sugar	In order to maintain control of your diabetes, you manage your blood sugar level through medication, diet, and exercise. / Your blood sugar mostly stays within a target range that is not considered hypoglycaemia (too low) or hyperglycaemia (too high). / ○ If your blood sugar level is too low, you may experience dizziness/light-headedness, sweating, or shaking. / ○ If your blood sugar level is too high, you may experience tiredness, blurred vision, thirst, or frequent urination.
Mealtime Insulin	You give yourself insulin injections around mealtimes.
Long-Acting Insulin (once each week)	You give yourself an injection of long-acting insulin once each week.
Blood Sugar Fluctuations (mostly steady within target range)	Your blood sugar levels are generally in control with your insulin. / Your morning blood sugar is generally within your target range, but it varies from day to day. / Your average blood sugar levels are good, but throughout the day, you often have times when your blood sugar levels are higher or lower within your target range.

Results

Sample Description
- A total of 289 participants completed interviews, including 86 participants with T1D and 203 participants with T2D (**Table 1**).

Health State Rankings and Preferences
- Preference scale results are presented in **Table 2**.
- Almost all participants with T1D (97.7%) preferred low GV over high GV, although two participants with T1D (2.3%) reported no preference.
- Low GV was also preferred over high GV by nearly all participants with T2D (99.5%). One participant with T2D (0.5%) reported no preference
- Common reasons for preferring low GV included stress, worry, and exhaustion associated with high GV (**Table 3**).
- The small number of respondents with no preference between the health states expressed that the health states were not meaningfully different from one another since the blood glucose levels in both states were within target range (**Table 3**).

Table 1. Demographic and Clinical Characteristics

Characteristics	Type 1 Diabetes (N=86)	Type 2 Diabetes (N=203)	Total Sample (N=289)
Age (years), Mean, (SD)	36.6 (13.3)	55.1 (11.0)	49.6 (14.5)
Gender, n (%)			
Male	37 (43.0%)	103 (50.7%)	140 (48.4%)
Female	48 (55.8%)	98 (48.3%)	146 (50.5%)
Nonbinary	1 (1.2%)	2 (1.0%)	3 (1.0%)
Current medication for diabetes, n (%)			
Oral medication only	-	149 (73.4%)	149 (51.6%)
Insulin only	78 (90.7%)	7 (3.4%)	85 (29.4%)
Non-insulin injectable medication only	-	1 (0.5%)	1 (0.3%)
Oral medication and insulin	8 (9.3%)	23 (11.3%)	31 (10.7%)
Oral medication and non-insulin injectable medication	-	17 (8.4%)	17 (5.9%)
Insulin and non-insulin injectable medication	-	2 (1.0%)	2 (0.7%)
Oral medication, insulin, and non-insulin injectable medication	-	2 (1.0%)	2 (0.7%)
Other medication only	-	2 (1.0%)	2 (0.7%)
Route of administration for current insulin, n (%)			
Injection	50 (58.1%)	34 (100.0%)	84 (70.0%)
Pump	35 (40.7%)	-	35 (29.2%)
Both injection and pump	1 (1.2%)	-	1 (0.8%)
Time since diabetes diagnosis (years), Mean (SD)	18.1 (12.1)	8.9 (7.3)	11.7 (9.9)

Abbreviations: SD = standard deviation; T1D = type 1 diabetes; T2D = type 2 diabetes

Table 2. Health State Preference Rating Scale[a]

	N	Preference Rating, n (%)						
		Prefer "mostly steady within target range"			No preference	Prefer "varies within target range"		
		Strongly	Moderately	Slightly		Slightly	Moderately	Strongly
Total Sample	289	207 (71.6%)	57 (19.7%)	22 (7.6%)	3 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
T1D	86	58 (67.4%)	18 (20.9%)	8 (9.3%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
T2D	203	149 (73.4%)	39 (19.2%)	14 (6.9%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

[a] Preference Rating Scale for Glycemic Variability Health States: "Please select the number on the scale below that best describes your preference between "mostly steady within target range" and "varies within target range."
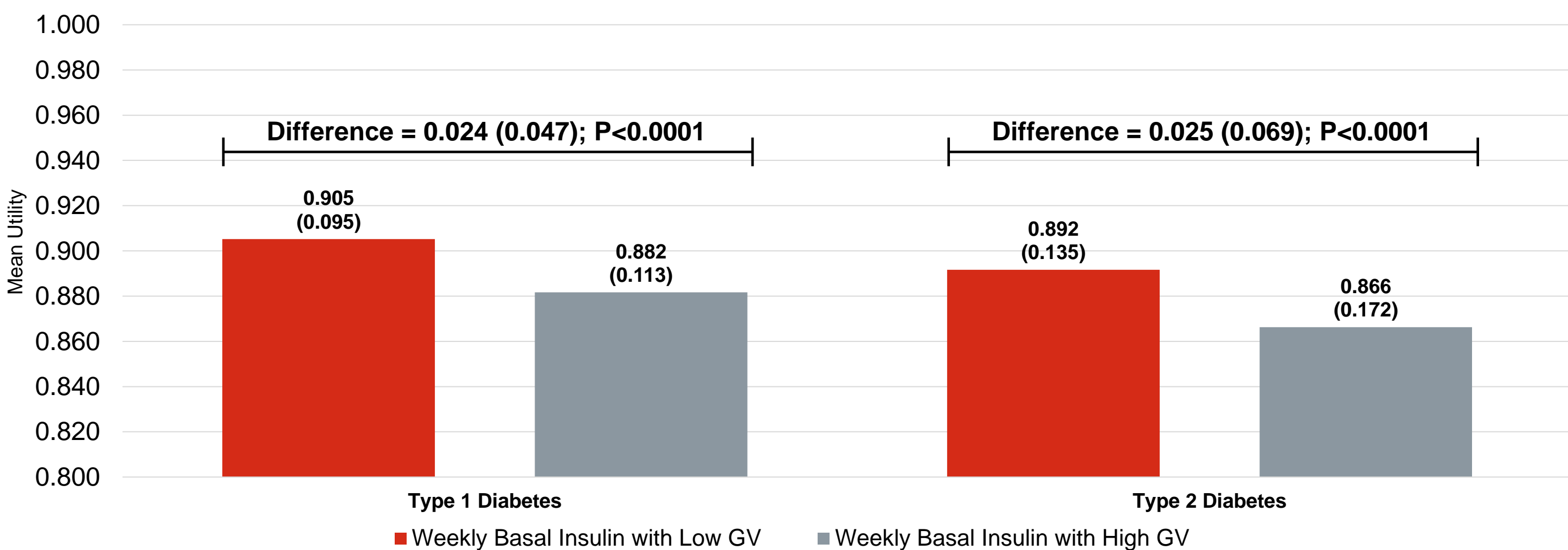
Table 3. Illustrative Quotations Explaining Preferences for GV Health States

Quotes from participants preferring "mostly steady within target range" (n=286)	Quotes from participants with no preference (n=3)
101-005 (T1D): "When the level is steady, I feel a lot better particularly emotionally…Even when it is in the normal range, fluctuations can have a big impact."	**201-026 (T1D):** "There is really no difference. It would be a coin toss between them…If it's within target range, you shouldn't be having symptoms…Overall, the average HbA1c would be the same…I'd be delighted with both."
101-008 (T1D): "Fluctuations really stresses me out so controlling this is very important to my mental health."	**202-006 (T2D):** "I don't really know what effect that [high GV] is having on you." (Interviewer noted that participant did not think it was an issue since not in hypoglycemia or hyperglycemia range)
102-016 (T2D): "I wouldn't be worrying about my blood sugar, and I could eat and drink stuff with less worry."	**301-020 (T1D):** "I don't feel like there is a real difference in the way to live your life…For both you still have the anxiety that you have diabetes, and you can still go low."
202-012 (T2D): "If you are up and down during the day even in the target range you will still have different energy levels. So, it's better to be balanced."	

Health State Utilities
- Mean (SD) utilities are presented in **Figure 2**.
- Weekly basal insulin with low GV was associated with a higher utility than weekly basal insulin with high GV among patients with T1D (utility difference = 0.024; $P < 0.0001$) and T2D (utility difference = 0.025; $P < 0.0001$).

Figure 2. Mean (SD) Health States Utilities Associated with GV

Type 1 Diabetes: Difference = 0.024 (0.047); P<0.0001 — Weekly Basal Insulin with Low GV: 0.905 (0.095); Weekly Basal Insulin with High GV: 0.882 (0.113)

Type 2 Diabetes: Difference = 0.025 (0.069); P<0.0001 — Weekly Basal Insulin with Low GV: 0.892 (0.135); Weekly Basal Insulin with High GV: 0.866 (0.172)

■ Weekly Basal Insulin with Low GV   ■ Weekly Basal Insulin with High GV

Limitations
- The utilities for GV resulting from this study represent the specific health states rather than actual patient experience. The extent to which these utilities might differ from values reported by patients who have actually used weekly insulin is not known.
- GV is a broad concept that includes many types of variability. This study included a general description of "variability within target range" and did not include glucose excursions that are out of target range.

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